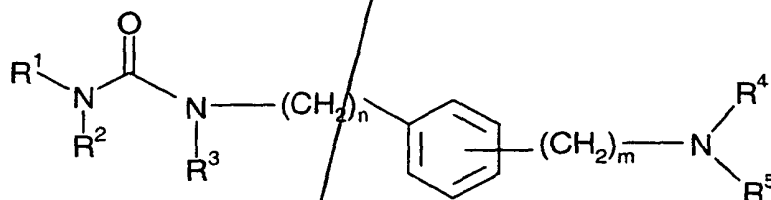


CLAIMS

1. A compound according to formula I



wherein

m and n is each and independently an integer of from 1-3, and one or more of the hydrogens in such an alkylene-chain may optionally be substituted by any one of

10 C₁ - C₆ alkyl, C₁ - C₆ alkoxy, or hydroxy; *or*

one or more of the methylene groups may optionally be substituted by a heteroatom such as O, N or S;

15 R¹ is selected from hydrogen, a branched or straight C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₈ cycloalkyl, C₄-C₈(alkyl-cycloalkyl) wherein the alkyl is C₁-C₂ alkyl and the cycloalkyl is C₃-C₆ cycloalkyl;

R² is selected from any of

20

(i) hydrogen;

(ii) a straight or branched C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

25

(iii) -[(CH₂)_q- aryl];

(iv) $-(\text{CH}_2)_r$ - heteroaryl] where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;

and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below; and wherein q and r is each and independently an integer of from 0 to 3;

(v) C_3 - C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;

and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) C_6 - C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

or

R^1 and R^2 may optionally form a heterocyclic ring;

R^3 is selected from anyone of

(i) hydrogen;

(ii) a straight or branched C_1 - C_6 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl;

(iii) $-(\text{CH}_2)_q\text{-aryl}$] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is
5 as defined below;

(iv) heteroaryl- $(\text{C}_5 - \text{C}_{10}$ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as
10 defined below;

(v) $\text{C}_3\text{-C}_{10}$ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally
15 and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) $-(\text{C}_3\text{-C}_6 \text{ cycloalkyl})\text{-(CH}_2)_q$] wherein q is an integer of from 1 to 3;

20 R^4 is selected from

(i) hydrogen,

(ii) a straight or branched $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl or $\text{C}_2\text{-C}_6$ alkynyl;

25 (iii) $-(\text{CH}_2)_q\text{-aryl}$] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl

may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(iv) heteoaryl-(C₅ - C₁₀ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(v) C₃-C₁₀ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) C₆-C₁₀ aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

R⁵ is selected from anyone of

(i) hydrogen;

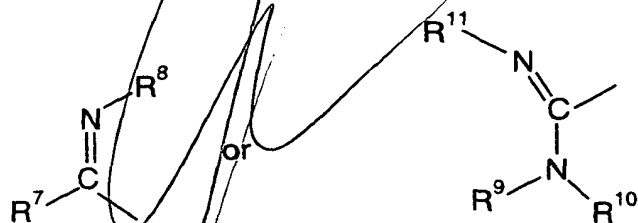
(ii) a straight or branched C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

(iii) $-(\text{CH}_2)_q\text{-aryl}$ wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(iv) heteroaryl- $(\text{C}_5 - \text{C}_{10}$ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(v) $\text{C}_3\text{-C}_{10}$ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi)



wherein

$\text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ and R^{11} is each and independently selected from

(a) hydrogen;

(b) a straight or branched C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl;

5 (c) -[(CH₂)_q-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

10 (d) heteroaryl-(C₅ - C₁₀ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

15 (e) C₃-C₁₀ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

20 (f) C₆-C₁₀ aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

25 or

R⁴ and R⁵ may optionally form a heterocyclic ring;

Y is each and independently selected from any of hydrogen, CH_3 ; $-(\text{CH}_2)_{p_1}\text{CF}_3$;
 halogen; C_1 - C_3 alkoxy; hydroxy; $-\text{NO}_2$; $-\text{OCF}_3$; $-\text{CONR}^a\text{R}^b$; $-\text{COOR}^a$;
 $-\text{COR}^a$; $-(\text{CH}_2)_{p_2}\text{NR}^a\text{R}^b$; $-(\text{CH}_2)_{p_3}\text{CH}_3$, $(\text{CH}_2)_{p_4}\text{SOR}^a\text{R}^b$; $-(\text{CH}_2)_{p_5}\text{SO}_2\text{R}^a$;
 5 $-(\text{CH}_2)_{p_6}\text{SO}_2\text{NR}^a$; C_4 - C_8 (alkyl-cycloalkyl) wherein alkyl is C_1 - C_2 alkyl and
 cycloalkyl is C_3 - C_6 cycloalkyl; 1 or 2 heteroaryl(s) having from 5 to 10 atoms and
 the heteroatom(s) being selected from any of S, N and O; and oxides such as
 N-oxides or sulfoxides; and wherein

10 R^a and R^b is each and independently selected from hydrogen, a branched or straight
 C_1 - C_6 alkyl, C_1 - C_6 alkenyl, C_3 - C_8 cycloalkyl; and wherein
 p^1 , p^2 , p^3 , p^4 , p^5 and p^6 is each and independently 0, 1 or 2;

as well as pharmaceutically acceptable salts, isomers, hydrates, isoforms and prodrugs
 15 thereof.

2. A compound according to formula I of claim 1, wherein
 $m=n=1$

20 R^1 is selected from

- (i) hydrogen;
- (ii) a branched or straight C_1 - C_6 alkyl; or
- (iii) C_3 - C_8 cycloalkyl;

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R² is selected from any of

(i) hydrogen;

(ii) a straight or branched C₁-C₆ alkyl;

5

(iii) -[(CH₂)_q- aryl];

(iv) -[(CH₂)_r- heteroaryl] where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;

and wherein the aryl and heteroaryl may optionally and independently be substituted by
10 1 or 2 substituents Y where each Y is as defined in claim 1; and wherein q and r is each and independently an integer of from 0 to 3;

(v) C₃-C₆ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and
15 the heteroatom being selected from any of S, N and O;

and wherein the aryl and heteroaryl may optionally and independently be substituted by
1 or 2 substituents Y where each Y is as defined in claim 1;

(vi) C₆-C₁₀ aryl, optionally and independently be substituted by 1 or 2 substituents Y
20 wherein each Y is as defined in claim 1;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted
25 by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

or

R¹ and R² may optionally form a heterocyclic ring;

R³ is selected from any one of

(i) hydrogen;

5 (ii) a straight or branched C₁-C₆ alkyl;

(iii) $-(\text{CH}_2)_q\text{-aryl}$ wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl
10 may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteroaryl-(C₅ - C₁₀ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may
15 optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) C₃-C₁₀ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom
20 being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(vi) $-(\text{C}_3\text{-C}_6\text{ cycloalkyl})\text{-(CH}_2)_q$ wherein q is an integer of from 1 to 3;

25

R⁴ is selected from

(i) hydrogen;

(ii) a straight or branched C₁-C₆ alkyl;

(iii) $-(\text{CH}_2)_q\text{-aryl}$] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl
5 may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteroaryl- $(\text{C}_5 - \text{C}_{10}$ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may
10 optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) $\text{C}_6\text{-C}_{10}$ aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O
15 and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

R^5 is selected from anyone of

20

(i) hydrogen;

(ii) a straight or branched $\text{C}_1\text{-C}_6$ alkyl;

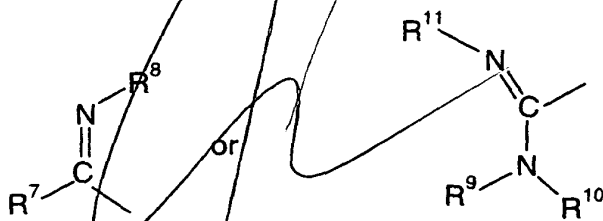
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(iii) $-(\text{CH}_2)_q\text{-aryl}$] wherein q is 0 or 1, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteroaryl- $(\text{C}_5 - \text{C}_{10}$ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) $\text{C}_3\text{-C}_6$ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(vi)



wherein

R^7 , R^8 , R^9 , R^{10} and R^{11} is each and independently selected from

(a) hydrogen;

(b) a straight or branched $\text{C}_1\text{-C}_6$ alkyl or $\text{C}_2\text{-C}_6$ alkenyl;

(c) $-(\text{CH}_2)_q\text{-aryl}$ wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(d) heteroaryl-($\text{C}_5 - \text{C}_{10}$ alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(e) $\text{C}_3\text{-C}_{10}$ cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(f) $\text{C}_6\text{-C}_{10}$ aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

or

R^4 and R^5 may form a heterocyclic ring which may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1.

a 3. A compound according to claim ²⁴ 7, wherein
 $m=n=1$

5 R^1 is selected from

- (i) a straight or branched C_1 - C_6 alkyl; ^{or}
 (ii) C_3 - C_8 cycloalkyl;

R^2 is selected from

- 10 (i) methyl; ^{or}
 (ii) phenyl optionally substituted by 1 or 2 substituents Y wherein each Y is as defined in
a claim ²³ 1;

15 R^3 is selected from

- (i) $-CH_2$ -phenyl, optionally substituted by 1 or 2 substituents Y where Y is as defined in
 claim ²³ 1;

- (ii) $-CH_2$ -cyclohexyl *or* $-CH_2$ -cyclopentyl;

20

R^4 is selected from

- (i) hydrogen; ^{or}
 (ii) methyl;

25

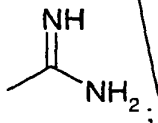
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R^5 is selected from

(i) hydrogen;

(ii) methyl; *or*

5 (iii)

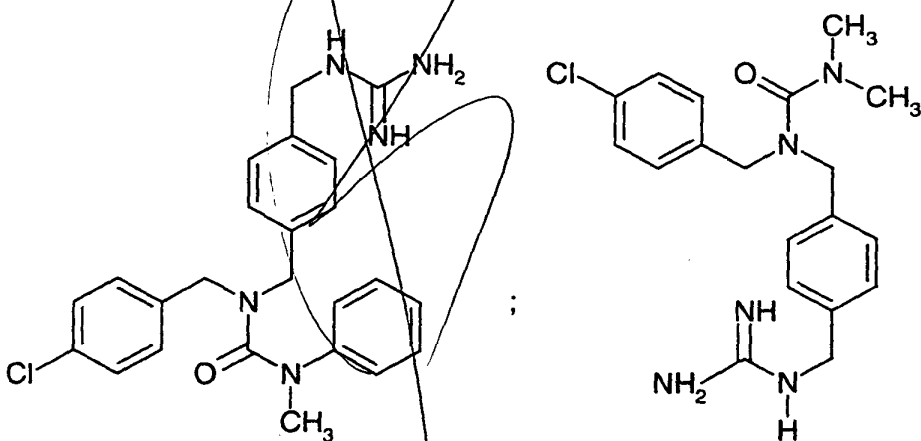


or

10 R^4 and R^5 together form a heterocyclic ring, optionally substituted by 1 or 2 substituents Y, where Y is as defined in claim 1. ²³

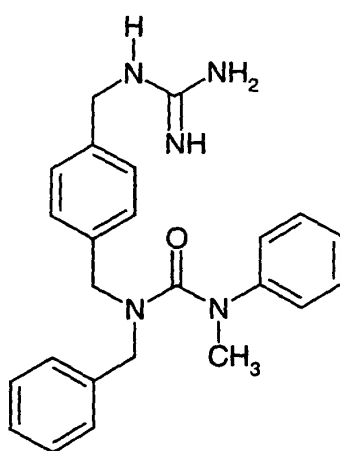
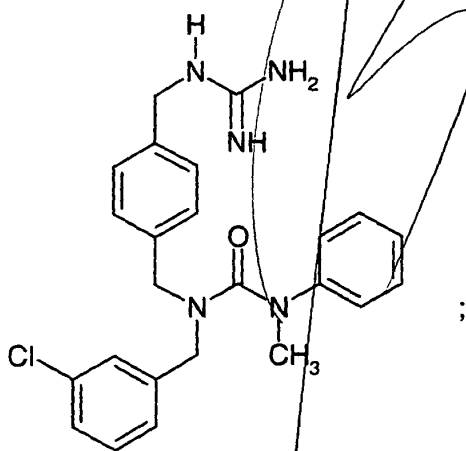
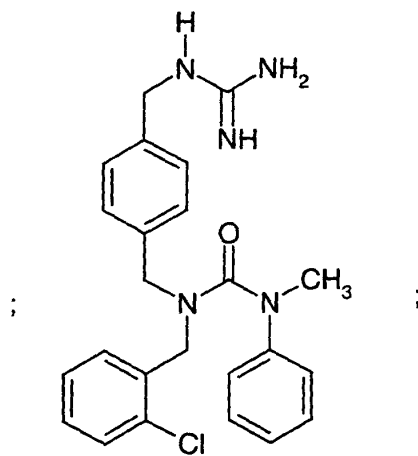
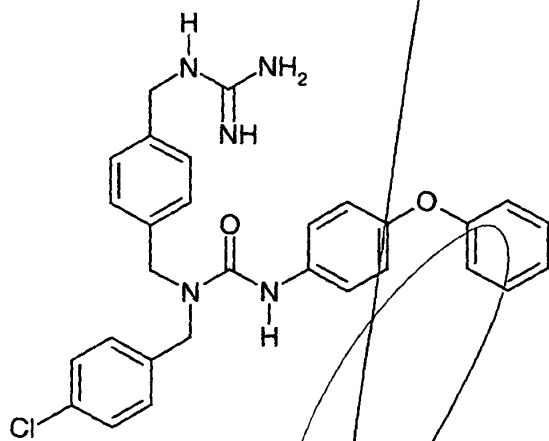
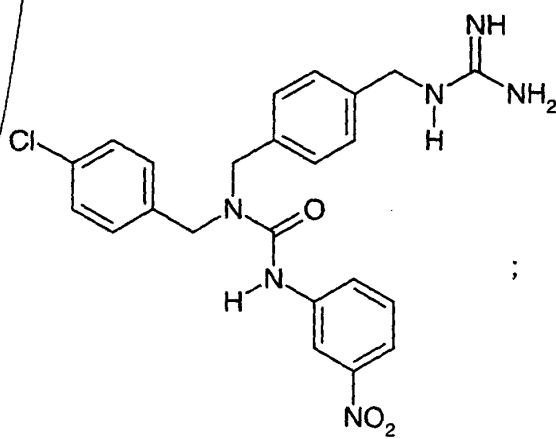
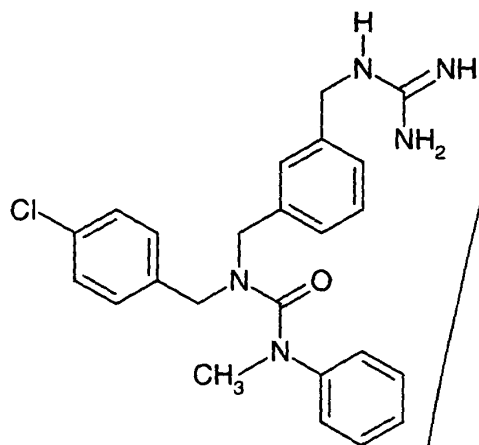
4. A compound ^{wherein said} according to claim 1, which compound is ~~any one~~ selected from ;

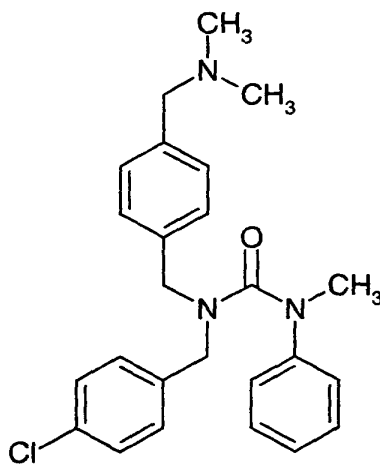
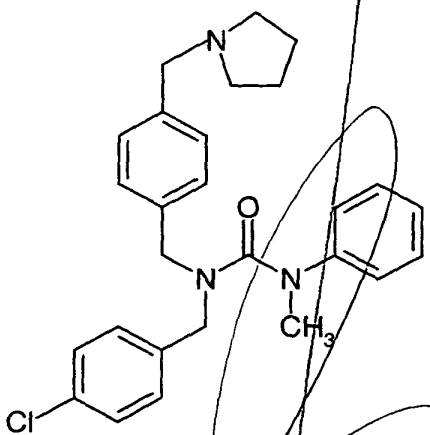
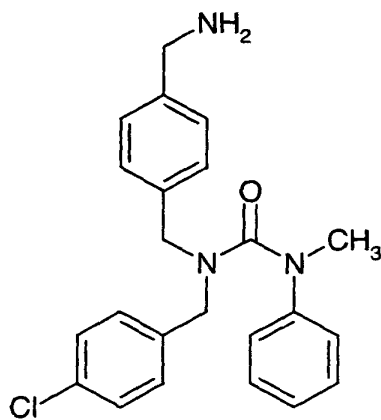
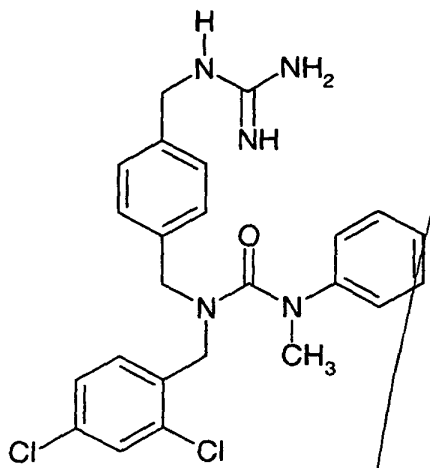
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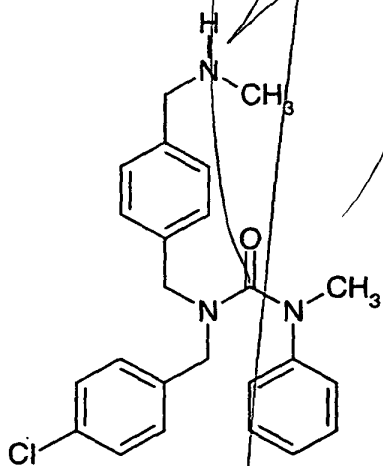
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5. A compound according to any of the preceding claims, in form of its hydrochloride, sulfate, tartrate or citrate salts.
- 5 6. A compound according to any of claims 1-5 for use in therapy.
7. A compound according to claim 6, wherein the therapy is pain management.
8. A compound according to claim 6, wherein the therapy is directed towards gastrointestinal disorders.
- 10 9. A compound according to claim 6, wherein the therapy is directed towards spinal injuries.
- 15 10. A compound according to claim 6, wherein the therapy is directed to disorders of the sympathetic nervous system.
11. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of pain.
- 20 12. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of gastrointestinal disorders.
13. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of spinal injuries.
- 25 14. A compound according to any of claims 1-10, further characterised in that it is isotopically labelled.
- 30 15. Use of a compound according to claim 14 as a diagnostic agent.

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Suh
a2

a

16. An isotopically ^{labeled} ~~labeled~~ compound of the formula I of claim ²³ ~~1~~.

17. A diagnostic agent comprising a compound of the formula I of claim 1.

5

a

a

18. A pharmaceutical composition comprising a compound of the formula I according to claim ²³ ~~1~~ as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.

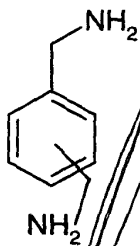
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19. A process for the preparation of a compound of the formula I according to claim 1, whereby

A)

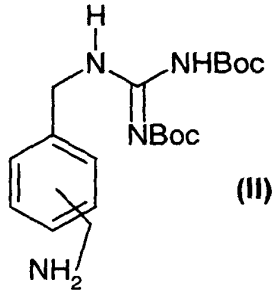
(i) bis-amino xylylene of the formula

15

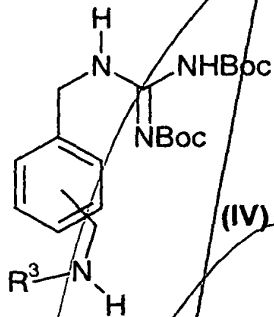


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is converted into mono-(diBoc)-guanidinomethyl of the formula (II)

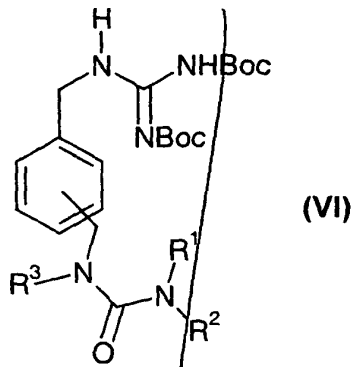


5 which thereafter is reacted with an aldehyde, providing a secondary amine of the general formula IV

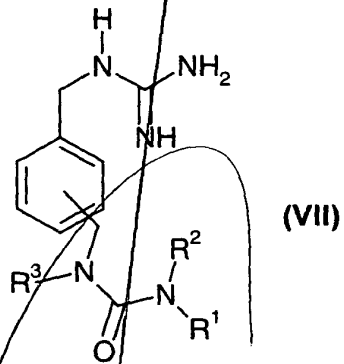


10 wherein R³ is as defined in formula I of claim 1;

(ii) compound IV is subjected to an urea formation, providing a compound of the formula (VI)



which finally is deprotected, providing a compound of the general formula VII



5 wherein

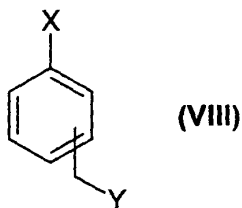
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R^1 , R^2 and R^3 are as defined in formula I of claim 1; or

B)

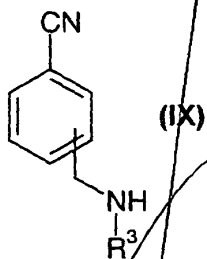
(i) a compound of the formula (VIII)

5

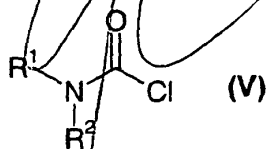


wherein X is CN and Y is CHO, is subjected to a reductive amination using a primary amine R^3NH_2 wherein R^3 is as defined in formula I of claim 1, providing a compound of the formula (IX)

10

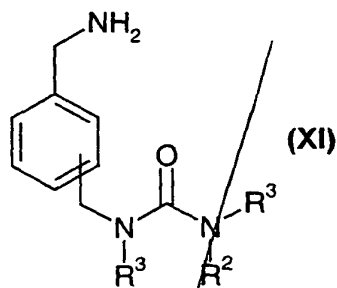


wherein R^3 is as defined in formula I of claim 1, which thereafter is subjected to an urea reaction by using a chloroformate of the formula (V)



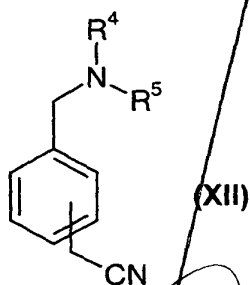
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which finally is reduced, providing a compound of the formula (XI)

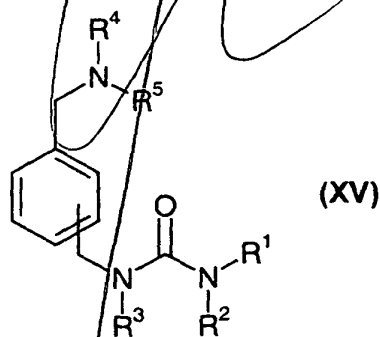


; or

(ii) compound (VIII) wherein X is CH_2Br and Y is CN , is reacted with an amine $\text{R}^4\text{R}^5\text{NH}$ wherein R^4 and R^5 are as defined in formula I of claim 1, providing a compound of the formula (XII)



which is reduced and reacted with an aldehyde R^3CHO wherein R^3 is as defined in formula I of claim 1, and finally subjected to an urea action with a chloroformate (V) as in step (i), providing a compound of the formula (XV)



wherein R^1 , R^2 , R^3 , R^4 and R^5 are as defined in formula I of claim 1.

*Sub
3
a*

5

20. A method for the treatment of pain, whereby an effective amount of a compound of the formula I according to claim 1 is administered to a subject in need of pain management.

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21. A method for the treatment of gastrointestinal disorders, whereby an effective amount of a compound of the formula I according to claim 1, is administered to a subject suffering from said gastrointestinal disorder.

22. A method for the treatment of spinal injuries, whereby an effective amount of a compound of the formula I according to claim 1, is administered to a subject suffering from said spinal injury.

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